CHEMICALS UNDER CONSIDERATION FOR POSSIBLE LISTING VIA THE AUTHORITATIVE BODIES MECHANISM

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The chemicals listed in the following table may meet the criteria for the listing of carcinogens formally identified by an authoritative body, as set forth in Title 22, California Code of Regulations, Section 12306. Information on the occurrence and usage of the chemicals and the relevant references to the authoritative body publications are also given. A summary of the results of relevant carcinogenicity studies of these chemicals follows the table.

Chemical	CAS No.	Identity of chemical	Reference
Nitromethane	75-52-5	Chemical stabilizer, solvent, intermediate; fuel or fuel additive; component of explosives mixtures for mining, oil-well drilling, etc.	NTP (1995a; 1995c)
Tetrafluoroethylene	116-14-3	Used in synthesis of Teflon	NTP (1995b; 1995c)
Vinyl Fluoride	75-02-5	Used in production of polyvinyl fluoride and other fluoro-polymers	IARC (1995)

Summarized below are the relevant carcinogenesis studies and conclusions for chemicals under evaluation as potentially having satisfied the criteria for listing under the authoritative bodies provision of Proposition 65, as set forth in 22 CCR Section 12306. Documents published by the National Toxicology Program (NTP) and International Agency for Research on Carcinogens (IARC), two Proposition 65 authoritative bodies, were the primary sources for the summary. The statements in bold reflect data and conclusions that may satisfy the criteria for the sufficiency of evidence for carcinogenicity in subsection (e) Section 12306. The evidence for the carcinogenicity of the chemical is only briefly discussed here. The full citations for the primary source documents are given in this report. The primary source documents, on file at OEHHA, provide additional details on the critical studies described below.

Nitromethane (CAS No. 75-52-5)

Positive cancer bioassays in two species, with multiple sites in mice.

The National Toxicology Program (NTP, 1995a; 1995c) has concluded that there is clear evidence of carcinogenic activity of nitromethane in female F344/N rats and in male and female $B6C3F_1$ mice.

NTP (1995a) administered nitromethane to F344/N rats and $B6C3F_1$ mice by inhalation for two years. In female rats exposed to nitromethane, incidences in mammary gland fibroadenoma, fibroadenoma or adenoma (combined) and fibroadenoma, adenoma or carcinoma (combined) increased with increasing exposure concentration. The incidences of fibroadenoma, adenoma or carcinoma (combined) were 21/50, 25/50, 34/50 and 41/50 for control, low-, mid- and high-dose animals, respectively. In mid- and high-dose groups, incidences were significantly greater than those in controls.

In both male and female mice, the incidences of Harderian gland adenoma and adenoma or carcinoma (combined) increased with increasing exposure concentration. Statistically significant increases in Harderian gland adenomas or carcinomas (combined) were observed in mid- and high-dose groups (males: 10/50, 11/50, 25/50, 37/50; females: 6/50, 9/50, 20/50, 21/50). A neoplasm of the Harderian gland is considered to be an indicator of tumorigenic potential.

Nitromethane exposure also caused a significant increase in the incidences of alveolar/bronchiolar tumors in both male and female mice. In male mice, the incidence of alveolar/bronchiolar adenoma or carcinoma (combined) was 13/50, 13/50, 12/50, and 20/50 for control, low-, mid-, and high-dose animals, respectively. In female mice, the incidence of alveolar/bronchiolar adenoma or carcinoma (combined) was 3/50, 6/50, 6/50 and 12/50 for control, low-, mid- and high-dose groups, respectively. The incidences of hepatocellular adenomas and adenomas or carcinomas (combined) were increased in low- and high-dose female mice. The incidences of hepatocellular adenomas or carcinomas (combined) in females were 19/50, 34/50, 22/50, and 40/50 for control, low-, mid- and high-dose groups, respectively.

NTP found no evidence of carcinogenic activity of nitromethane in male F344/N rats.

These findings were published in a draft technical report and were subsequently reviewed and accepted at the December 5-6, 1995 NTP Technical Reports Review Subcommittee Meeting as reported in the *Summary Minutes* for that meeting (NTP, 1995c).

Tetrafluoroethylene (CAS No. 116-14-3)

Positive cancer bioassays in both sexes of two species.

NTP (1995b; 1995c) concluded that there is clear evidence of carcinogenic activity of tetrafluoroethylene in male and female F344/N rats and in male and female B6C3F$_1$ mice.

NTP (1995b) exposed F344/N rats and B6C3F$_1$ mice to tetrafluoroethylene by inhalation for two years. In rats, tetrafluoroethylene exposure resulted in significantly increased incidences of renal tubule adenomas or carcinomas (combined) in high-dose males (3/50, 5/50, 9/50, 13/50) and females (0/50, 3/50, 3/50, 10/50). Tetrafluoroethylene exposure also resulted in increases in hepatocellular adenomas and carcinomas (combined) which were statistically significant in mid-dose males (4/50, 7/50, 15/50, 8/50) and in female rats in all exposed groups (0/50, 7/50, 12/50, 8/50). In addition, the incidence of hepatic hemangiosarcomas in mid-dose females was significantly greater than in controls (0/50, 0/50, 5/50, 1/50). The historical incidence of this uncommon neoplasm in NTP inhalation studies is 0.3%. Tetrafluoroethylene exposure also resulted in statistically significant increases in the incidence of mononuclear cell leukemia in female rats in all exposed groups (16/50, 31/50, 23/50, 36/50).

The NTP (1995b) study in B6C3F$_1$ mice was terminated early (95 weeks) due to poor survival. The reduction in survival was considered to be the result of animals dying from tetrafluoroethylene-related hepatic neoplasms. These included hemangiomas, hemangiosarcomas and hepatocellular adenomas and carcinomas. The incidences of hepatic hemangiosarcoma in all exposed groups of males and females were significantly greater than those in controls, and the incidences occurred with a significant positive trend in males and females. The incidences of hemangiomas and hemangiosarcomas (combined) were highly significant and occurred with a positive trend for exposed groups of males (0/48, 26/48, 30/48, 38/48) and females (0/48, 31/48, 28/47, 35/47). Both neoplasms are uncommon in mice. Incidences of hepatocellular carcinomas and adenomas or carcinomas (combined) were significantly increased in males and females exposed to tetrafluoroethylene (males: carcinoma, 11/48, 20/48, 33/48, 26/48; adenoma or carcinoma combined, 26/48, 34/48, 39/48, 35/48; females: carcinoma, 4/48, 28/48, 22/47, 20/47; adenoma or carcinoma combined, 17/48, 33/48, 29/47, 28/47). In addition, the incidence of histiocytic sarcomas (all organs) was markedly increased in males and females exposed to tetrafluoroethylene (males: 0/48, 12/48, 7/48, 7/48; females: 1/48, 21/48, 19/47, 18/48).

These findings were published in a draft technical report and were subsequently reviewed and accepted at the December 5-6, 1995 NTP Technical Reports Review Subcommittee Meeting, as reported in the *Summary Minutes* for that meeting (NTP, 1995c).

Prior to the initiation of the NTP tetrafluoroethylene bioassays, IARC classified the chemical as a group 3 carcinogen (IARC, 1987).

Vinyl Fluoride (CAS No. 75-02-5)

Positive cancer bioassays in two species with multiple sites.

The International Agency for Research on Cancer (IARC, 1995) has identified vinyl fluoride as a Group 2A carcinogen based on sufficient evidence in experimental animals and the close structural similarity of vinyl fluoride to the known human carcinogen, vinyl chloride. Another closely related compound, vinyl bromide, was experimentally observed to be carcinogenic in animals. The three structurally related chemicals cause the same rare tumor (hepatic hemangiosarcoma) in experimental animals which is also caused by vinyl chloride in humans.

As cited by IARC (1995), Bogdanffy *et al*. (1995) exposed Sprague-Dawley rats to vinyl fluoride via inhalation for two years and reported increased incidences of hepatic hemangiosarcomas, hepatocellular adenomas and carcinomas, and Zymbal's gland tumors in both males and females. The incidence of hepatic hemangiosarcomas in female rats was 0/80, 8/80, 19/80, and 15/80 for control, low-, mid- and high-dose groups, respectively. In male rats, the incidence was 0/80, 5/80, 30/80 and 20/80 in the four groups, respectively.

The authors did not perform statistical analyses because of the differences in the sacrifice time (rats in each dose group were sacrificed when the number of survivors in that group declined to approximately 25% of the number at risk.)

As cited by IARC (1995), Bogdanffy *et al*. (1995) administered vinyl fluoride by inhalation to Swiss derived mice for up to 18 months. The study was terminated early due to dose-related mortality. Fatal hepatic hemangiosarcoma occurred in 1/81, 16/80, 42/80 and 42/81 males and 0/81, 13/81, 25/80 and 32/81 females in the control, low-, mid- and high-dose groups, respectively. Also observed were increased incidences of primary lung tumors (predominantly bronchioalveolar adenoma but some adenocarcinoma) in both males and females (males: 11/81, 45/80, 52/80, 56/81; females: 9/81, 24/80, 47/80, 53/81). In addition, the incidences of Harderian gland adenomas were markedly increased in both treated males and females (males: 3/66, 13/68, 12/66 and 31/62; females: 1/64, 7/61, 6/66, and 12/66) and the incidences of mammary gland neoplasms were increased in treated females (0/77, 22/76, 20/78 and 20/77). The authors did not perform statistical analyses because of the differences in the time of sacrifice (as described above).

References

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